DETAILED ACTION

1. Claims 1-2, 21-26, and 33-36 are currently pending in the instant application.

Response to Amendments and Arguments

2. Applicant's arguments and amendments filed 26 June 2008 have been fully considered and entered into the application. All rejections not explicitly maintained herein are withdrawn.

Maintained Claim Rejections- 35 U.S.C. § 112

(First Paragraph)

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The nature of the invention is a crystalline polymorph form A of Zolmitriptan, pharmaceutical compositions containing these forms, and methods of preparation. The state of the prior art is that the most useful method to compare X-ray powder diffraction data is to overlay and align the respective films and plots. The ensuing comparisons of peak positions and intensities will show whether the structures are the same or different (Byrn page 63). An x-ray diffraction pattern is like a "fingerprint" and Applicant has not provided why the certain peaks found in claim 1 are the only required peaks in the x-ray diffraction pattern that must match. There is no description

found in the specification why these certain claimed peaks are the only peaks required. The peaks present in the claims do not include all peaks of the x-ray diffraction pattern. The amount of direction present in the specification is the x-ray diffraction patterns of the claimed crystalline forms. Applicant has not provided why the entire "fingerprint" is not being claimed, nor does Applicant provide why only certain peaks are found in the claims and not others. The claims to only certain peaks do not find written description in the specification as the claims do not include the "fingerprint" and the specification fails to provide any description as to why the data claimed is characteristic of the claimed forms and why the entire "fingerprint" is not required. While there is some description for characteristic peaks found on pages 2 and 3, there is no written description provided as to why these peaks are considered characteristic. Therefore, claim 1 is rejected as there is no written description as to why the data present is the only data required from the "fingerprints" to distinguish the claimed forms from other forms.

Applicant's representative asserts that the art cited in this regard (Byrns, page 63) related to the practical method of evaluating x-ray diagrams and that it does not teach that the correlation of each and every peak of such a diagram is necessary, since the person skilled in this art knows very well that an x-ray diagram may contain peaks unrelated to the subject and the more intensive peaks are the more reliable ones. Furthermore, Applicant's representative asserts that these more reliable peaks have been claimed and therefore no explanation for this selection is necessary in the specification. Also, Applicant's representative is correct that instant claim 2 was added into this rejection as an inadvertent error, and the instant rejection of claim 2 has been withdrawn.

In response to the aforementioned arguments, Byrns, page 63, second paragraph, discusses peaks that occur in certain patterns. Byrns states, "...two patterns may show many differences but also have several peaks that appear to coincide. A judgment must be made as to whether the coincident peaks: 1) are indeed, just a few coincidences and the samples do have different structures; or 2) are due to the presence of a common component implying the sample is a mixture of structures." Because similar peaks can appear in two structurally different samples, it is important for the entire "fingerprint" to be claimed, rather than the most intense peaks as instantly claimed. This allows for ascertaining between two structurally similar compounds.

(Second Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 recites the limitation, "wherein the solution additionally contains a non-solvent selected from alkanes and ethers." The word "non-solvent" renders the claim indefinite because it is unclear to a person of ordinary skill in the art what "non-solvent" means. There is no definition in the specification, and claim 23 discloses alkanes and ethers as "non-solvents;" however, alkanes and ethers are generally used as solvents or solvent mixtures in the chemical arts. (See Handbook of Solvents, Wypych, section 3.3.1 on hydrocarbons and 3.3.9 on ethers).

Applicant's representative points to the paragraph bridging pages 12 and 13 of the instant specification for the definition of "non-solvent." This paragraph provides exemplifications of

various "non-solvents" as claimed; however, does not provide a definition for the term "non-solvent." Finally, when searching for the definition of non-solvent online, the word "insolvent" is listed. Insolvent is defined as: unable to meet debts or discharge liabilities; bankrupt. There is no clear definition for "non-solvent."

Maintained Claim Rejections- 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-2 and 25-26 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Patel (U.S. Patent No. 6,084,103).

Claims 1 and 2 are directed to a crystalline polymorph A of formula (S)-4-[[3-[2-(diemthylamino)ethyl]-1H-indol-5-yl]methyl]-2-oxazolidinone (chemical name for Zolmitriptan) with a certain X-ray powder diffraction pattern and peak intensity as claimed. Patel teaches the preparation of (S)-4-{3-[2-(diemthylamino)ethyl]-1H-indol-5-yl]methyl}-2-oxazolidinone in Example 1, Stage 6A.

Applicant's representative asserts that Patel is totally silent as to the crystal form of the solid product, Zolmitriptan. It is true that the reference does not teach a specific crystalline form of Zolmitriptan, because the inherent feature that defines such form (e.g. XRD, IR, etc.) is not disclosed. Thus, the difference between the prior art solid and the instantly claimed crystalline form lies on characteristics for which the reference happens to be silent. This is not ordinary

inherency; however, as stated in Ex parte Anderson, 21 USPQ 2nd 1241 and 1251 "There is ample precedent for shifting burden to an Applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its manufacture." Furthermore, MPEP 2112.V states that, "once a reference teaching product appearing to be substantially identical is made the basis of a rejection, and the Examiner presents evidence or reasoning tending to show inherency, the burden shifts to the Applicant to show an unobvious difference."

Claim 25 is directed to a process of preparing a crystalline polymorph A of (S)-4-{3-[2-(diemthylamino)ethyl]-1H-indol-5-yl]methyl}-2-oxazolidinone wherein crystalline Zolmitriptan is suspended, or amorphous Zolmitriptan is dispersed, in an organic solvent, provided that the organic solvent does not contain 1-butanol, anisole, ethyl methyl ketone, tetrahydrofuran, or 1,4-dioxone. Patel teaches, (Example 1, Stage 6A, columns 12 and 13, lines 59 and 2 respectively), the use of ethyl acetate as a solvent, as well as the chilling of the suspension. At the end of the procedure, when the solvent is distilled off and the suspension is cooled and then dried, the process of crystallization is occurring, prior to the purification of the product.

Claim 26 discloses a process of claim 25 wherein the organic solvent is an alcohol or an acetate. As discussed above in the rejection of claim 25, the organic solvent is ethyl acetate as taught in Patel (Example 1, Stage 6A, column 12, line 59).

Applicant's representative asserts that claims 25 and 26 either disperses amorphous Zolmitriptan or suspends crystalline Zolmitriptan in a solvent and does not dissolve Zolmitriptan as taught in Patel et al.

Patel et al. does teach a suspension in the process for preparing the instantly claimed crystalline form as is evidenced in column 13, line 2, wherein the suspension is cooled. From this disclosure of Patel et al., it is inherent that crystalline Zolmitriptan must have been suspended at some point for a suspension to be present in Stage 6A. Also, it is important to mention that dissolve and disperse are synonymous (thesaurus.com).

New Claim Rejections - 35 U.S.C. § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 35 discloses a pharmaceutical composition comprising the crystalline polymorphic form A of Zolmitriptan and a pharmaceutically acceptable carrier. The only component present in the polymorph is the crystal lattice. Once hydrated, as in the case when a carrier is added, a second component will change the equilibrium and ultimately the composition of the crystalline polymorph form of the compound. By placing the crystalline polymorph form A of Zolmitriptan in a carrier to yield a pharmaceutical composition, it would actually rehydrate the polymorph resulting in a loss of form, and ultimately yielding the Zolmitriptan compound as disclosed in Patel (claim 1, formula 1).

Claim 36 discloses Zolmitriptan containing a crystalline polymorphic form A according to claim 1. As stated above in the rejection of claim 1, Examiner cannot differentiate between Zolmitriptan and the Zolmitriptan crystalline form based on the compound characteristics

provided. Patel teaches Zolmitriptan by the chemical name of (S)-4-{3-[2-(diemthylamino)ethyl]-1H-indol-5-yl]methyl}-2-oxazolidinone in claim 1, formula I.

Claim Objections

7. Claim 2 is objected to for depending on a rejected base claim.

Conclusion

8. Claims 21-22, 24, and 33-34 are allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

10. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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